REMARKS

The 35 U.S.C. § 103 Rejection

Claims 42-54 stand rejected under 35 U.S.C. § 103 as being allegedly unpatentable over U.S. Patent No. 5,112,734 (Kramer et al.) and 5,043,272 (Hartley et al.). This rejection is respectfully traversed.

The Office Action cited the Summary and columns 5-10 of Kramer et al. In the Summary, it is stated: This invention pertains to an improved method for detecting *a* nucleic acid target sequence... (lines 43-45) In col. 7, lines 21-22, it is stated: The replicated RNA is then detected as indicative of the presence or the amount of target sequence." Furthermore, in col. 10, there are two important statements describing the method and its results: The method can be used to detect specific genes, gene segments of RNA molecules (lines 5-7). Amplification is obtained by exponential replication of the replicatable RNA (lines 34-35). Upon close inspection, the undersigned could not find a mention of the claimed "linearly amplified RNA copies" or of "relative representation of the specific nuclei acid messages within the sample." Applicants agree that Kramer et al do not teach a multigene expression profile.

The Office Action cited columns 3-7 and 9-10 of Hartley et al. Hartley discloses amplifying nucleotides by using a pool of random primers. The undersigned could not find any mention of linear amplification. The only time linearity was mentioned was in reference to linear viral material to be amplified (10:55, 11: 42, 11: 69 and 13: 11). In fact, the patent warns: "If the primer is not of random sequence, its sequence must be of sufficient diversity to prime at multiple sites along the template nucleic acid sequence, since the degree of amplification may be proportional to the number of priming sites." (5:59:-63) Apparently the random primers may hybridize multiple times to some sequences and not at all to other sequences, resulting in larger numbers of the multiply hybridized sequences and none of the un-hybridized sequences. Thus, the relative abundance of a message would vary with the numbers of random primers hybridizing to a given message. This indicates that one could not expect Hartley et al. to produce linear expansion "wherein the amplified specific nucleic acid messages each have an abundance which reflects the relative representation of specific nucleic acid messages within the samples." (claim 42)

To summarize, the above patents individually or in combination do not teach "a collection of linearly amplified specific nucleic acid messages, wherein said amplified

specific nucleic acid messages each have an abundance which reflects the relative representation of specific nucleic acid messages within the sample." (claim 42 and dependent claims 43-51) Neither do they disclose "a collection of linearly amplified specific nucleic acid messages, wherein said amplified specific nucleic acid messages have been amplified simultaneously with RNA polymerase and primer linked to RNA polymerase promoter." (claim 53 and dependent claim 54) Moreover, it would not have been obvious to combine a technique for amplifying a single target (Kramer) with a technique for amplifying many sequences and portions of sequences (Hartley). Applicants respectfully request that this ground for rejection be withdrawn.

The Office Action next rejected claims 43-51 and 54 under 35 USC 103(a) as being unpatentable over Kramer et al. and Hartley et al. as applied to claims 43, 45-51, 54 and 54 above, and further in view of US 5,466,788 (Alquist et al.) which cites to the use of RNA-dependent RNA polymerase and RNA molecule containing the subgenomic promoter and the structural gene (4: 41-44). The Office Action cited columns 4-5 and 9. Nowhere in those columns was the undersigned able to find the production of multiple genes at one time. Moreover, the single specific message was amplified exponentially, as indicated in the paragraph on alphaviruses and the Sindbis-like viruses "(+) strand RNA molecules outnumber the full-length (-) strand template about 100 to 1." (2:32-33)

In summary, none of the references alone or in combination appear to teach "a collection of linearly amplified specific nucleic acid messages, wherein said amplified specific nucleic acid messages each have an abundance which reflects the relative representation of specific nucleic acid messages within the sample." (claim 42 and dependent claims 42-52) Neither do they disclose "a collection of linearly amplified specific nucleic acid messages, wherein said amplified specific nucleic acid messages have been amplified simultaneously with RNA polymerase and primer linked to RNA polymerase promoter." (claims 53-54) Moreover, it would not have been obvious to combine a technique for amplifying a single target (Kramer and Ahlquist) with a technique for amplifying many sequences and portions of sequences (Hartley). Applicants respectfully request that this ground for rejection be withdrawn.

The argument set forth above is equally applicable to the dependent claims. The independent claims being allowable, the dependent claims must also be allowable.

In view of the foregoing, it is respectfully asserted that the claims are now in condition for allowance.

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Request for Allowance

It is believed that this Amendment places the above-identified patent application into condition for allowance. Early favorable consideration of this Amendment is earnestly solicited.

If in the opinion of the Examiner, an interview would expedite the prosecution of this application, the Examiner is cordially invited to call the undersigned attorney at the number indicated below.

Respectfully submitted,
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